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Autoantibodies in Moroccan patients with type 1 diabetes: Which one to choose?

ABSTRACT

Background. Immunological investigations are intended for diagnosing T1D in atypical clinical presentation, also exploring the predisposition to T1D in a context of multiple autoimmune disorders or among the siblings of a patient with type 1 diabetes. While the diagnosing or the screening of T1D using five antibodies presents high expenses especially in emerging countries, it is for interest to determine their prevalence in order to choose the most frequent and most relevant. The aim of our study is to determine the prevalence of antibodies in Moroccan population.

Methods. We investigated 62 T1D patients, the prevalence of autoantibodies was 74% for glutamic acid decarboxylase 65 auto-antibody (GADA), 46% for insulinoma-associated protein 2 autoantibody (IA2A), and 3% for islet cell antibodies (ICA). GADA and/or IA2A were reported in all patients (100%). The GADA frequency was neither associated with the duration of diabetes nor the age of patients.

Results. Finally, GADAs are by far the best markers for T1D, IA2As complements GADAs and increases the diagnostic sensitivity for detection of pancreatic autoimmunity and ICA should be abandoned because of its low prevalence. (Clin Diabetol 2021; 10)

Key words: Moroccan type 1 diabetes, pancreatic autoimmunity, pancreatic autoantibodies, GADA, IA2A, ICA

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Clinical Diabetology 2021, 10

DOI: 10.5603/DK.a2021.0030

Received: 15.10.2020

Accepted: 01.01.2021

Introduction

Type 1 diabetes (T1D) is the result of a destructive inflammatory process of the pancreatic β cells and the final consequence is insulinopenia noting that pancreatic antibodies (Ab) are considered markers and not actors of this cell destruction. The antibodies test is important to make an etiological diagnosis of diabetes in atypical clinical presentation, moreover, to study the predisposition in first-degree family members of a patient with T1D and in a context of multi-organ autoimmunity. There are five types of anti-pancreatic antibodies: glutamic acid decarboxylase 65 auto-antibody (GADA), insulinoma-associated protein 2 autoantibody (IA2A), islet cell antibodies (ICA), insulin autoantibodies (IAA) and recently Zinc Transporter 8 antibody (ZnT8A). Given the high cost of the five antibodies, especially in emerging countries, our study aspires to provide evidence about their prevalence in Moroccan T1D and therefore to choose the most frequent and most relevant one.

Materials and methods

A cross-sectional study of patients with T1DM was conducted in the endocrinology department of Moulay Ismail military hospital in Meknes, Morocco, for the period extending from January 2016 to June 2019. All T1D patients were included. We collected demographic parameters (age, sex, age of discovery and duration of diabetes) and serological parameters (GADA, IA2A and ICA) which were analyzed using an electrochemiluminescence technique on the standardized fully automated MAGLUMI CLIA analyzer. ZnT8A has not been performed because it is not available and IAA has not been performed because patients are not insulin naive. An exclusion criteria for this study was the absence of laboratory confirmation of autoimmunity (negative immunoassay). The study was approved by their local ethics committees and all patients gave informed consent.

Table 1. Demography and autoantibodies of patients with T1D

Cases	Sex (M/F)	Age at diagnosis [years] (mean) Range	Duration of diabetes [years] Range	GADA	IA2A	ICA	GADA and/or IA2A
62	47/17	17 (1–36)	8 (0–32)	46/62	26/62	2/62	62/62

GADA — glutamic acid decarboxylase; IA2A — insulinoma-associated protein 2 autoantibody; ICA — islet cell antibodies

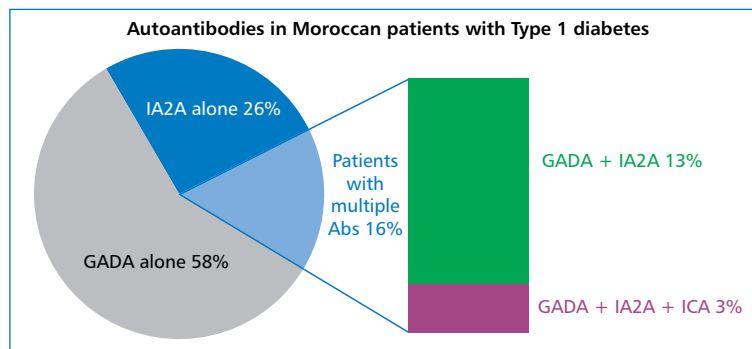


Figure 1. The distribution of autoantibodies in Moroccan patients with type 1 diabetes. Abs — antibodies; GADA — glutamic acid decarboxylase; IA2A — insulinoma-associated protein 2 autoantibody; ICA — islet cell antibodies

Table 2. Prevalence of autoantibodies according to age at diagnosis of T1D

Frequency of antibodies group	GADA	IA2A	ICA	GADA and/or IA2A
Children (16/62)	88% (14/16)	44% (7/16)	6% (1/16)	100% (16/16)
Adults (46/62)	70% (32/46)	41% (19/46)	2% (1/46)	100% (46/46)

Statistical analysis was performed with SPSS (Statistical Package for the Social Sciences) version 23 statistic software package. Data were expressed as means \pm standard deviation (SD). Comparisons between groups were performed with analysis of non-parametric test. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 62 patients, 47 men and 15 women were included, after excluding 10 patients with negative pancreatic autoimmunity. The mean age at diagnosis was 17 years and the mean duration of diabetes was 8 years. The prevalence of Ab was 74% for GADA, 42% for IA2 and only 3% for ICA. GADA and/or IA2A were reported in all patients (100%). Table 1 and Figure 1 show-distribution of all autoantibodies.

We analyzed the prevalence of autoantibodies at different ages at diagnosis, in the adult population

(46/62), 32 patients had GADA (70%) and 19 patients had IA2A (41%), while in children (16/62), we found 14 cases with GADA (88%) and 7 cases with IA2A (44%). Table 2 summarizes the distribution of auto-antibodies by age. The mean duration of diabetes was 8 years (0 to 32 years), and we chose two groups of T1D to analyze the association between prevalence of antibodies and diabetes duration. In the 26 recent diabetes patients (disease duration ≤ 1 year), GADA were present in 22 cases (85%) and 10 cases for IA2A (38%), while in the 36 patients with long duration of diabetes (> 1 ans), 24 had GADA (67%) and 16 had IA2A (44%) (Table 3). Increased frequency of antibodies was not associated with younger age or recent diabetes

Discussion

Pancreatic autoantibodies are used in current diabetology practice to make an etiological diagnosis of diabetes in an atypical clinical presentation, as well

Table 3. Prevalence of autoantibodies according to duration of T1D

Frequency of antibodies group	GADA	IA2A	ICA	GADA and/or IA2A
Recent onset diabetes (26/62)	85% (22/26)	38% (10/26)	4% (1/26)	100% (26/26)
Long duration diabetes (36/62)	67% (24/36)	44% (16/36)	3% (1/36)	100% (36/36)

GADA — glutamic acid decarboxylase; IA2A — insulinoma-associated protein 2 autoantibody; ICA — islet cell antibodies

as to define the predisposition of T1D in first-degree family members of a patient with T1D. There are five types of anti-pancreatic antibodies: GADA, IA2A, ICA, IAA and ZnT8A. We did not test the IAA in our study due to the fact that most of the patients were already on insulin therapy neither was ZnT8 since it is not available in our platform [1]. To our knowledge the frequency of these CAs has not been evaluated in the Moroccan or North African population, hence the interest of this study. GADAs autoantibody is present in approximately 60 to 80% in all the populations studied of T1D, they were considered to be the best marker of pancreatic autoimmunity. Overall the GADA prevalence in our series (74%) was consistent with that reported in the Caucasian population (60-80%). In the Asian population they are the most represented but with a lower prevalence (30–47%) [2, 3].

In our study, GADA prevalence was higher in children and adolescents compared to adults (88% versus 68%) and most studies share the same finding [4–6]. However, increased frequency was not statistically associated with younger age in our study and a minority of authors have reported that age does not affect the test results [3, 7].

By analyzing diabetes duration and antibodies prevalence, we have demonstrated that the detection sensitivity of GADA is very high at 85% in the presence of recent diabetes against 67% for long duration diabetes. Considering the spread of our population according to the diabetes duration (8 years on average and 8 years of standard deviation), we observed a perfect agreement with the opinion who said that GADA declines more slowly [2, 3, 8].

IA2As were present in 50 to 80% of T1D within one year after diagnosis in Caucasian populations whereas they are considered to be weak markers in Asian population (< 40%) which is similar to our results (38%). This low prevalence is not modifiable regardless of the diabetes duration or the younger age [3, 8, 9].

The real surprise in our population is that we still have near zero prevalence of ICA, while it is around 50% in some series [3, 10] So we think that the ICA test should be abandoned in our context.

Limitations

The main limitation of our monocentric study is the small sample size and large age spread of our population study. Further multicenter studies should be carried and focus on the measurement of ZnT8A.

Conclusion

The prevalence of GADA or IA2A varies in different ethnicities. This is the first study that examined the prevalence of anti-pancreatic antibodies in Moroccan population. In our population GADAs are by far the best markers for T1D diagnosis, and even though the IA2As are considered weak tests in comparison with GADA they are still a second choice test, they increase the detection sensitivity. We think that ICA should be abandoned because of its low prevalence. Finally, we are impatiently awaiting for the availability of ZnT8A in our platform to be able to compare them with other pancreatic autoantibodies.

Conflict of interest

The authors declare no competing of interests.

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